PLACENTAL TRANSPORT OF PCDD's AND PCDF's IN HUMANS

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ABSTRACT

Concentration of PCDD's and PCDF's are compared in liver and fat of nursed and not nursed human infants. It appears that there is placental transport of these compounds in humans. However, the amount that is thus transported to the foetus is small compared with the amount obtained by nursing.

INTRODUCTION

In the environment there are various sources of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD's and PCDF's). Humans are exposed to these substances mainly in food, especially food of animal origin with a high fat content (1,2). In the body PCDD's and PCDF's accumulate mainly in fat and, at a lower level, in the liver (3). One way to eliminate PCDD's and PCDF's from the body is by way of mothers milk. Mothers milk contains considerable amounts of the toxic 2,3,7,8-substituted PCDD/PCDF congeners (4). A child nursed with mothers milk is exposed to rather high concentrations of dioxins and dibenzofurans (5). Little is known about the amount of PCDD's and PCDF's that enter the unborn infant by placental transport. In Marmoset monkeys the rate of placental transport appears to be very low for the majority of 2,3,7,8-substituted congeners (6).

In this paper we will discuss PCDD/PCDF levels in human infants. Data from fat and liver samples of stillborn foetuses and a five-day old child, who was

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not nursed are compared with data for a child who was nursed for three months. Analytical data for a human placenta will also be discussed.

MATERIALS AND METHODS

Human samples

Human samples were taken from children who died at the time of birth or some time after, at the academic hospital of the University of Amsterdam (AMC). Liver samples of each infant and fat samples of the nursed and not nursed child (H7 and H5) were analysed. A placenta sample was also analysed. The samples are listed in table 1.

Table 1. Human tissue samples used in this work.

Sample	description		
	age	duration of pregnancy	nursing
H1-H4		31 to 36 weeks	
H5	5 days	34 weeks	no
H7	3 months		yes
Placenta	normal pregnancy, healthy child.		

Clean-up and analysis of PCDD's and PCDF's

The fat and liver samples were freeze-dried. A mixture of ten ^{13}C-PCDD/F's was added as internal standard. The samples were extracted with toluene for 24 hours; the clean-up involved GPC treatment and liquid chromatography on silicagel/conc. H_2SO_4 and basic alumina (7). The analysis of the samples was perfomed on GC-MS (VG70 250s, resolution 10.000, temperature programm: 180°C 2min, 3°C/min to 260°C, 260°C 19min).

RESULTS AND DISCUSSION

PCDD's and PCDF's were found, especially the 2,3,7,8-substituted congeners, in all samples. Table 2 gives the concentrations of the most important congeners. High concentrations were observed only for several 2,3,7,8-substituted congeners (especially 2,3,4,7,8-P_5CDF, 1,2,3,4,7,8 and 1,2,3,6,7,8-H_6CDF, H_7CDF, 1,2,3,6,7,8-H_6CDD, H_7CDD and OCDD). OCDF was on the detection level (variable 1(fat)-15(liver)pg). 2,3,7,8-T_4CDD and some non-toxic congeners were found in the blank control; this determines the deteccion level

of these congeners. Liver contents of the foetuses and the not-nursed infant are low compared to that of the nursed child.

Table 2: PCDD and PCDF concentration in liver and adipose tissue of infants and in a placenta.

Congener	Concentration (pg/g wet wt)						
	fetus liver[1] (H1-4) (n=4)		infant (H5)[2]		infant (H7)[3]		Placenta
			liver	fat	liver	fat	
2378-T_4CDD	0.23	(0.16)[4]	0.03[4]	3.4[4]	0.29	3.98	0.26
12378-P_5CDD	0.09	(0.05)	0.07	2.13	0.58	6.93	0.53
123478-H_6CDD	0.09	(0.02)	0.04	n.d.	0.49	3.18	0.21
123678-H_6CDD	0.29	(0.22)	0.16	7.07	2.77	28.98	0.42
123789-H_6CDD	0.07	(0.02)	0.03	n.d.	0.52	2.95	0.08
1234678-H_7CDD	1.03	(0.87)	0.29	12.33	6.84	10.00	0.59
OCDD	8.8	(6.4)	3.87	87.40	67.94	105.11	4.22
23478-P_5CDF	0.12	(0.09)	0.12	5.20	2.47	14.66	1.01
123478-H_6CDF	0.12	(0.03)	0.04	n.d.	2.09	2.61	0.17
123678-H_6CDF	0.10	(0.04)	0.04	n.d.	2.74	2.05	0.12
1233478-H_7CDF	0.10	(0.05)	0.09	1.80	5.39	4.43	0.18

[1] Mean of four samples (standard deviation)
[2] Not nursed
[3] Nursed
[4] Unfortunately, TCDD was also found in the blank control; the absolute amount in these samples was very low and matches the cont rol concen tration.

The results indicate that there is a placental transport of PCDD's and PCDF's in humans. However, the exposure to PCDD's and PCDF's by way of mothers milk is much more important. The same conclusion was drawn from an experiment with Marmoset monkeys, where a pregnant female was given a mixture of PCDD's and PCDF's (s.c.) and the infants were analysed at birth or after a 33 day nursing period (6). In that experiment the liver concentrations of congeners in the foetuses (not nursed) was about one tenth of the congener concentration in adipose tissue of the adult. For 2,3,7,8-T_4CDD and 1,2,3,7,8-P_5CDD a higher concentration in the foetuses was found. If the human data presented here are compared with data for adult fat content of PCDD's and PCDF's (4,8,9), it appears that, in general, the human data match the marmoset findings. The presence of TCDD in the blank control makes it uncertain if there is also a higher placental transport of TCDD in humans, than for the other congeners.

The pattern of the PCDD's and PCDF's in the samples matches that of which is found in human milk and blood (4,8). In the placenta the amount of PCDD/PCDF congeners exceed that of human blood several times, indicating a moderate accumulation of these substances.

CONCLUSION

The data indicate that placental transport of PCDD's and PCDF's takes place in humans. However, the rate of this 'vertical' transport is small compared with exposure by way of mothers milk. Unfortunately, no data for PCDD/PCDF concentrations in the tissues of the infants' mothers were available. In experiments following this preliminary work tissue concentrations of the mother will be considered.

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